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TITLE: Emergency Preservation and Resuscitation for Cardiac Arrest from Trauma (EPR-CAT)

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14. ABSTRACT

During this second year of the project our efforts have continued to focus on the regulatory aspects of this complex clinical trial. We communicated directly with regulatory experts in the US Army and the US Food and Drug Administration (FDA). We have successfully obtained an Investigational Device Exemption from the FDA Center for Devices and Radiological Health Office of Device Evaluation. We subsequently received approval of the proposal from the University Pittsburgh Institutional Review Board (IRB) as the coordinating center for the trial. The local investigators at the University of Maryland have submitted the proposal to their IRB. They are in the process of responding to questions raised by the IRB, particularly about their plans for community consultation and public disclosure. We have formed the Data Safety and Monitoring Board for this trial. In December, 2008, we conducted the first training session for EPR at the University of Maryland. We have collected retrospective data on trauma patients who underwent emergency department thoracotomies in order to develop the most appropriate inclusion and exclusion criteria for subject selection for this trial. So far, this data has not yielded novel information to revise our protocol.

15. SUBJECT TERMS
Trauma, hemorrhagic shock, cardiac arrest, cardiopulmonary resuscitation, hypothermia

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Introduction
Cardiopulmonary resuscitation (CPR) can save victims of normovolemic cardiac arrest (CA), e.g., ventricular fibrillation. During exsanguination CA from trauma, however, CPR, even with an emergency department (ED) thoracotomy and open chest CPR, doesn't work. *Emergency Preservation and Resuscitation (EPR)* was developed to rapidly preserve the organism during ischemia, using hypothermia, drugs, and fluids, to "buy time" for transport and resuscitative surgery. The purpose of this study is to test the feasibility of rapidly inducing profound hypothermia ($\leq 10^{o}C$) with an aortic flush in trauma victims that have suffered CA and failed standard resuscitative efforts to enable resuscitative surgery and delayed resuscitation with cardiopulmonary bypass. The primary outcome variable will be survival to hospital discharge with minimal neurologic dysfunction.

Body
Scientific Progress
In December, 2008, we conducted the first training session for EPR at the University of Maryland. Representatives from the University of Arizona and Massachusetts General Hospital were also present. The training involved 2 large animal experiments and cadaver dissection.

Given the complexity of our planned intervention for trauma patients in cardiac arrest, we need to optimize subject inclusion and exclusion criteria. The literature on such patients is scant, with studies focusing on mortality rates and crude information such as signs of life (pulse, breathing, spontaneous movements) in the field or emergency department and admission cardiac rhythm. To better define this patient population to optimize subject selection, we have initiated a retrospective study at several centers to look at other factors that could be quickly determined during the resuscitation of a trauma patient in the emergency department. This retrospective study should produce publishable data, although so far we have not obtained sufficient data to make any conclusions.

Administrative and Logistic Matters
The first regulatory step for proceeding with this study was to obtain an Investigational Device Exemption (IDE) from the Food and Drug Administration (FDA). Our trial is complicated by the fact that both fluids and equipment are to be used for an application that is not currently approved by the FDA. We have now obtained an investigator-sponsored IDE from the FDA Center for Devices and Radiological Health Office of Device Evaluation.

With the approval of the IDE, we were able to obtain approval for the proposal from the University of Pittsburgh Institutional Review Board (IRB) as the coordinating center for the study, with the plan to have the University of Maryland be the first center to enroll patients. The investigators at the University of Maryland have submitted the proposal to their IRB and are in the process of responding to the Board's questions. The investigators at the University of Pennsylvania are working on agreements with their administration and their cardiothoracic surgeons regarding participation in the study.

Simultaneously, we have begun the process of human use approval from the DoD. An early draft proposal was reviewed by Louise M. Pascal, RN, MS, Senior Human Subjects Protection Scientist (AMDEX Corporation), Human Research Protection Office (HRPO), Office of Research Protections (ORP), U.S. Army Medical Research & Materiel Command (USAMRMC). They can not formally review the proposal until we have approval from the IRB at a participating institution, including the plans for community consultation and public disclosure.

Key Research Accomplishments
The most important accomplishments this past year have been the receipt of the IDE from the FDA, the approval from the University of Pittsburgh IRB as a coordinating center, and the formation of the DSMB. In addition, the completion of the first training session for implementation of EPR helped solidify the technical plans for implementation and how to train personnel at participating sites.

We have begun to collect retrospective data from each site on patients who underwent Emergency Department thoracotomies, presumably potential candidates for resuscitation by EPR. Theses databases are just the beginning of the information that we will need to revise our initial inclusion criteria for the proposed EPR study.

Reportable Outcomes
As this year's efforts have focused on the regulatory and training issues, there has not been any new research data to report.

Conclusion
Most of the work so far on this project has been focused on the regulatory process. We have an IDE and approval for a coordinating center. We also have successfully conducted a training session. The next steps are to obtain approval from the IRB at the University of Maryland, followed by submission of the proposal to the USAMRMC. In the mean time, we will continue to gather data on current experience with patients who develop a cardiac arrest from trauma and could be candidates for the EPR trial. To this end, we are also exploring the potential for obtaining data from the Resuscitation Outcomes Consortium studies of prehospital care in patients with life-threatening injuries.

References
None

Appendicies
None